# PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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Date: 19 APR 2004
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PCT
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WRITTEN OPINION
(PCT Rule 66)

| | |
|---|---|
| Date of mailing *(day/month/year)* | 16.04.2004 |
| Applicant's or agent's file reference: P32590WO/NCB | **REPLY DUE** **within 3 month(s)** from the above date of mailing |

| International application No. | International filing date *(day/month/year)* | Priority date *(day/month/year)* |
|---|---|---|
| PCT/GB 03/03192 | 25.07.2003 | 26.07.2002 |

International Patent Classification (IPC) or both national classification and IPC
C12N15/62

Applicant
ROSLIN INSTITUTE (EDINBURGH) et al.

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

| | | |
|---|---|---|
| I | ☒ | Basis of the opinion |
| II | ☐ | Priority |
| III | ☐ | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| IV | ☐ | Lack of unity of invention |
| V | ☒ | Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| VI | ☐ | Certain documents cited |
| VII | ☐ | Certain defects in the international application |
| VIII | ☐ | Certain observations on the international application |

3. The applicant is hereby **invited to reply** to this opinion.

**When?** See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

**How?** By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

**Also:** For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.
For an informal communication with the examiner, see Rule 66.6.

**If no reply is filed,** the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 26.11.2004


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## I. Basis of the opinion

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed")*:

**Description, Pages**

1-49 as originally filed

**Claims, Numbers**

1-15 received on 01.03.2004 with letter of 26.02.2004

**Drawings, Sheets**

1/21-21/21 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:
   - ☐ the drawings, sheets:

5. ☐ This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

6. Additional observations, if necessary:

**V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | |
|---|---|---|
| Novelty (N) | Claims | 1, 11 (NO) |
| Inventive step (IS) | Claims | 1-11 (NO) |
| Industrial applicability (IA) | Claims | 1-15 (?) |

2. Citations and explanations

**see separate sheet**

**Additional remarks to section V:**

**1. Novelty (Article 33(2) PCT)**

1.1 The present application discloses the use of a nucleic acid construct, comprising a sequence encoding a lipocalin, for the detection of a gene activation event resulting from a change in a cell. Said change may be toxicological stress, a metabolic change or a disease.

1.2 The documents mentioned in this communication are numbered as in the International Search Report (ISR), i.e. D1 corresponds to the first document of the ISR etc.

1.3 The present application does not satisfy the criterion set forth in Article 33(2) PCT because the subject matter of claims 1 and 11 is not novel in view of document D17. Claim 1 relates to the use of a nucleic acid construct comprising a sequence encoding a member of the lipocalin protein family. It does not specify how said construct is used. Thus claim 1 also encompasses a use in which the construct is used as a hybridization probe for detecting activation of the lipocalin gene as induced by toxicological stress, metabolic change or disease (claim 11). Document D17 discloses (on p. 52, l. 28-34) the use of nucleic acids encoding lipocalins (probes) for the detection of a gene activation event (increased expression of the lipocalin encoding sequences) as induced by a toxic test compound. D17 also discloses the screening for compounds which alter the expression of the lipocalin (p. 44, l. 33 to p. 45, l. 34) by using (as a probe) a sequence encoding the lipocalin. Thus claim 1, as currently worded, and claim 11 is anticipated by D17.

**2. Inventive step (Article 33(3) PCT)**

2.1 It seems that none of the cited prior art documents discloses the use of a member of the lipocalin protein family as a reporter gene. Lipocalins are know in the art, their fusion with epitopes is known (e.g. in D1 or D7) but none of the documents suggests their usefulness as a reporter gene. Therefore it seems that the use of a lipocalin as a reporter gene, or a method of detecting gene activation using a

lipocalin reporter construct, can be considered inventive (claims 12-15).

2.2 The subject matter of claim 1, however, is not clearly defined in that the actual use is not defined: claim 1 does not state how the nucleic acid construct is used, there is no limitation that it is used as a reporter gene, or that it is transfected into the cell in which the gene activation event is tested. This also applies to claims 2-11.

3. **Industrial applicability (Article 33(4) PCT)**

The subject matter of claims 1-11 relates to a use for detection of a gene activation event in vitro or in vivo. Said gene activation event can be a disease. Thus the claims encompass a method of diagnosis performed in vivo on the human or animal body. The subject matter of claims 12-15 encompasses a method of diagnosis of a disease performed on a non-human animal. Thus the subject matter of claims 1-15 includes methods of diagnosis of the human or animal body and is thus excluded from examination by Article 34(4)(a)(i) PCT in combination with Rule 67(iv) PCT. For the assessment of these claims on the question whether they are industrially applicable, no unified criteria exist in PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject matter of claims to the use of a compound in medical treatment, but will allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment. The applicant is already informed that in the case of a European application, claims 1-15 do not seem to be allowable because 'diagnostic methods practised on the human or animal body shall not be regarded as inventions which are susceptible of industrial application'.